REMARKS

Claims 1-17 remain in the application. Claims 1, 3, 6, 7, and 10-17 are in independent form.

Pending claims 1-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,684,145 to Van Der Zee, et al. and Mittal, et al., as set forth in the final Office Action dated July 2, 2002. After filing a Supplemental Amendment under Rule 1.116, an Advisory Action was issued wherein the rejection under 35 U.S.C. § 103 was maintained for reasons of record. Specifically, the Advisory Action maintained that a skilled artisan would have had motivation for substituting the subunit portion of Van Der Zee, et al. with the BHV-1 gD of Mittal, et al. to protect cows against BHV-1. Further, the skilled artisan would have had a reasonable expectation for producing the claimed invention because Van Der Zee, et al. teaches that a strong immunogenic carrier is required to induce an immune response to GnRH and Mittal, et al. teaches that BHV-1 gD is a strong immunogen. Accordingly, the combined references account for the knowledge of the skilled artisan available at the time the invention was made and what would have been suggested to the ordinary artisan presumed to be familiar with the art.

It is undisputed that the Van Der Zee, et al. patent discloses a vaccine including a GnRH peptide conjugated to an *E. coli* fimbrial-fillament, wherein the vaccine elicits an immune response against GnRH. The Mittal, et al. reference discloses a recombinant form of gD from BHV-1 inserted into a human adenovirus type V vector.

The outstanding rejection involves a single issue with regard to rebutting a *prima facie* case of obviousness. As set forth in previous arguments, a fact-base explanation is needed as to why one of ordinary skill in the art at the time the invention was made would have been motivated to substitute the strong immunogenicity of BHV-1 gD taught by Mittal, et al. with the *E-coli* fimbrial subunit portion of the hybrid protein disclosed in the Van Der Zee, et al. patent to evoke an

immune response against GnRH and protect against BHV-1 infection. More specifically, there must be a reasonable expectation of success of achieving and maintaining the dual function of the hybrid protein after conjugation thereof. It is well known in the art, however, that the binding of proteins from two different sources can affect or functionally alter immunogenic sites, alter structural confirmation of either or both peptides, destroy functionality of either or both peptides, or make other expected and/or unexpected alternatives that result in a non-functional and/or non-immunogenic fused protein. In other words, it is well known to those of skill in the art that merely connecting any two proteins having individual functionality can be rendered non-functional once the two proteins are fused together.

As set forth in the declaration attached hereto and accompanying references (Bosch, et al. and Agterberg, et al.), it is demonstrated that the individual function of two individual proteins, when each protein is subsequently fused, cannot always be predicted. For example, in the references, PhoE is the studied protein. PhoE is an outer membrane protein with eight cell surface exposed regions. This protein also acts as a phage receptor. The exposed regions are predicted to serve as sites for insertion of foreign epitopes to make fusion proteins that allow display of both the epitope and the carrier (PhoE) at the cell surface and at the same time maintain the function of the PhoE protein as a phage receptor. However, Bosch, et al. and Agterberg, et al. prove that this prediction cannot be used to determine a priori which sites are suitable for insertion of foreign epitopes. (See, Bosch, et al. at page 488, "Discussion" Section, and Table 2; Agterberg, et al. at page 41, first column, page 43, second column, and page 44, second column). It can be seen that insertion at some exposed sites maintain the function of PhoE as an outer membrane protein, whereas insertion of epitopes at other exposed sites interferred with assembly of the PhoE into the outer membrane and its function as a phage receptor (Id.).

In light of the above arguments and references (Bosch, et al. and Agterberg, et al.), the fusion of any two proteins provides for an unpredictable result as to the individual functions of each fused proteins. It is merely speculation that the combination of any two proteins would result in a functional and/or active fused protein. In other words, in view of the cited prior art references and to those of ordinary skill in the art, that the combination of a strong immunogen as disclosed in Mittal, et al. and the *E.coli* fimbrial subunit as disclosed in Van Der Zee, et al., would not necessarily result in an immunologically active and functional protein capable of eliciting a specific and independent dual immunogenic response against the immunogen and the *E.coli* fimbrial subunit. In contradistinction to the Office Action's holding, the components of the claimed invention are merely mentioned in the cited prior art references. There is no suggestion in the prior art to combine the teachings disclosed in the cited prior art references so that the desired function of the presently claimed invention could be achieved. As is well known to those of skill in the art (as proven in the attached references and Declaration signed by a non-inventor), the resulting function of a fused protein is highly unpredictable since the binding of the proteins can affect and/or destroy functionality of either or both peptides.

As a result of these claimed differences over the cited prior art and lack of suggestion and motivation to modify the references or to combine the references, the present invention is patentably distinct. Reconsideration of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

The remaining dependent claims not specifically discussed herein are ultimately dependent upon the independent claims. References as applied against these dependent claims do not make up for the deficiencies of those references as discussed above. The prior art references do not disclose the characterizing features of the independent claims discussed above. Hence, it is respectfully submitted that all of the pending claims are patentable over the prior art.

In conclusion, it is respectfully submitted that the pending claims are in condition for allowance, which allowance is respectfully requested. In view of the foregoing remarks, reconsideration of the rejections and advancement of the case to issue are respectfully requested.

Applicants respectfully request to be contacted by telephone if any remaining issues exist.

The Commissioner is authorized to charge any fee or credit any overpayment in connection with this communication to our Deposit Account No. 11-1449.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" addressed to Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on June 27, 2003.

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